Docket Number: 037003-0280727

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re the Application of

GARY R. BRASLAWSKY et al.

Application No.: 10/058,069

Filed: January 29, 2002

Group Art Unit: 1642

Examiner: David J. Blanchard

Confirmation No.: 2502

For: ENGINEERED TETRAVALENT ANTIBODIES AND METHODS OF USE

TRANSMITTAL OF STATEMENT

UNDER § 152 OF THE ATOMIC ENERGY ACT

Mail Stop L & R
Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith is a statement under § 152 of the Atomic Energy Act, in response to the official communication mailed May 23, 2005. The attached document is timely filed within 30 days of the mailing of the request therefor by the Commissioner for Patents and Trademarks.

The present statement is being submitted as executed by three of the inventors. The assignee (Biogen Idec), after much diligence, has been unable to contact Inventor Braslawsky. Inventor Braslawsky is currently traveling through Europe. The assignee, through the undersigned attorney, will endeavor to reach Inventor Braslawsky in order that he may execute the document. Upon execution by Inventor Braslawsky, the statement will be resubmitted to the USPTO.

Respectfully submitted,

PILLSBURY WINTHROP SHAW PITTMAN LLP

By_____

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Docket Number: 037003-0280727
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GARY R. BRASLAWSKY et al. Group Art Unit: 1642

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STATEMENT UNDER § 152 OF THE ATOMIC ENERGY ACT

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Alexandria, VA 22313-1450

Sir:

This is in response to the official communication mailed May 23, 2005, requiring the applicants to file a statement under § 152 of the Atomic Energy Act within 30 days of the mailing of the request thereof by the Commissioner for Patents and Trademarks.

This response is timely filed within thirty days of the mailing of the official communication mailed May 23, 2005.

U.S. Patent Application No. 10/058,069
Attorney Ref. No.: 037003-0280727

Pursuant to Title 42 United States Code, section 2182, the applicants hereby declare as follows:

1. U.S. Patent Application No. 10/058,069 ("the '069 application") describes and claims the following invention:

• A dimeric antibody comprising a plurality of monomeric subunits wherein said monomeric subunits are non-covalently associated. A dimeric antibody according to the invention includes a tetravalent construct comprising two monomeric antibodies, at least one of which is modified by deletion of part or all of a constant region domain. A dimeric antibody according to the invention can be a homodimer or a heterodimer, and includes a dimeric antibody that reacts with an autoantigen or a tumor associated antigen. An embodiment of a dimeric antibody according to the invention can also be associated with a cytotoxic agent that comprises a radioisotope selected from the group consisting of ^{90}Y, ^{125}I, ^{131}I, ^{123}I, ^{111}In, ^{105}Rh, ^{153}Sm, ^{67}Cu, ^{67}Ga, ^{166}Ho, ^{177}Lu, ^{186}Re and ^{188}Re. (See, for example, pages 7-14, 22-25, and 30.)

• A method of treating a disorder in a mammal in need thereof comprising administering to said mammal a therapeutically effective amount of a dimeric antibody as described above. For example, an embodiment of the method of treating a disorder according to the invention includes a method wherein the dimeric antibody according to the invention is associated with a cytotoxic agent that comprises a radioisotope selected from the group consisting of ^{90}Y, ^{125}I, ^{131}I, ^{123}I, ^{111}In, ^{105}Rh, ^{153}Sm, ^{67}Cu, ^{67}Ga, ^{166}Ho, ^{177}Lu, ^{186}Re and ^{188}Re. The method of treating a disorder according to the invention includes a method wherein the disorder is an immune disorder or a neoplastic disorder. (See, for example, pages 30-48.)

• A kit useful for the treatment of a mammal suffering from or predisposed to a disorder comprising at least one container in which is deposited a dimeric antibody, and a label or an insert indicating that said dimeric antibody may be used to treat said disorder. (See, for example, pages 45-46.)

• A method for forming dimeric antibodies comprising the steps of: (i) culturing prokaryotic or eukaryotic host cells comprising DNA sequences encoding at least one modified antibody whereby the host cells produce a plurality of modified antibodies; (ii) allowing the plurality of modified antibodies to non-covalently associate whereby dimeric antibodies are formed; and (iii) recovering the dimeric antibodies from the host cell culture. (See, for example, pages 15-22 and 25-30.)

The description of the invention described by the '069 application that is stated above is a summary that is not intended to include every technical feature and embodiment and of the invention that is disclosed and claimed in the '069 application. Any technical features and

embodiments of the invention disclosed and claimed in the '069 application that are omitted from the summary above are considered by the applicants to be fully as patentable as those technical features and embodiments which are included in the above-stated summary.

2. The '069 application claims priority to the following three U.S. provisional patent applications:

(i) U.S. Provisional Application No. 60/341,858, filed December 21, 2001;
(ii) U.S. Provisional Application No. 60/331,481, filed November 16, 2001; and
(iii) U.S. Provisional Application No. 60/264,318, filed January 29, 2001.

As described in the specification of U.S. Provisional Application No. 60/341,858 ("the provisional '858 application"), which describes the same invention and discloses the same data and examples as the '069 application, the applicants made the surprising discovery that bivalent, monomeric domain-deleted antibodies are capable of associating non-covalently to form stable, tetravalent, dimeric antibodies (see Example 5, pages 52-53). The applicants discovered that such non-covalently assembled, tetravalent, dimeric antibodies bind their target antigens with significantly lower dissociation constant (Kd) than the bivalent, monomeric domain-deleted antibodies (see Example 7, pages 54-55) with the same antigen-binding domain. The applicants found that a bifunctional chelator capable of chelating a radioisotope can be conjugated to the non-covalently assembled dimeric antibodies, and that the resulting chelator-conjugated antibodies chelate radioisotopes to produce radiolabeled, non-covalently assembled, tetravalent, dimeric antibodies (see Example 6, pages 53-54, and Example 8, pages 56-57). The applicants demonstrated that radiolabeled, non-covalently assembled, tetravalent, dimeric antibodies have a beneficial tissue biodistribution in vivo (see Example 8, pages 56-57), and are expected to provide therapeutic benefit when administered to treat an immune disorder or a neoplastic disorder (see pages 45-46). The applicants also showed that unlabeled, non-covalently assembled, tetravalent, dimeric antibodies that bind specifically to a tumor associated antigen function effectively in vivo as anti-tumor agents (see Example 9, pages 57-58).

3. The discoveries and invention described in the provisional '858 application and in the non-provisional '069 application were made as a result of scientific research that was paid for by, and performed in the laboratories of, IDEC Pharmaceuticals, Inc., (now Biogen Idec, Inc.) in San Diego, CA, prior to December 21, 2001, the filing date of the provisional '858 application. The invention or discovery described in the provisional '858 application and in the non-provisional '069 application was not made or conceived in the course of or under any contract, subcontract, or arrangement entered into with or for the benefit of the Atomic Energy

Commission, regardless of whether the contract, subcontract, or arrangement involved the expenditure of funds by the Atomic Energy Commission.

4. IDEC Pharmaceuticals, Inc., merged with Biogen, Inc. in 2003, and the merged corporation changed its name to Biogen Idec Inc.

I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. §1001 and may jeopardize the validity of the application or any patent issued thereon.

Date	Gary R. Braslawsky
June 17, 2005 Date	Hanna Nabil
June 21, 2005 Date	Paul Chinn
June 17, 2005 Date	Kandasamy Hariharan